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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,890	08/13/2001	George B. McDonald	8105-011-US	8163

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1612	

MAIL DATE	DELIVERY MODE
02/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/928,890	MCDONALD ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action

Claims 1 and 4-15 are pending. No claim is allowed.

Summary of this Office Action dated February 3rd, 2008

1. Information Disclosure Statement
2. Copending Applications
3. Specification
4. 35 USC § 112 --- First Paragraph Written Description Rejection
5. Double Patenting Rejection
6. 35 USC § 103(a) Rejection
7. Response to Remarks
8. Conclusion
9. Communication

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Due to an inadvertent typing error supplemental action is as follows:

35 USC § 112 --- First Paragraph Written Description Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 4-15 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Following reasons apply:

Applicant had no possession of the method of treatment as claimed. Specification contains no example, description, teaching or guidance so that one skilled in the art to make and use the invention. Claimed invention has not been disclosed for such a treatment with "atleast two oral dosage forms of beclomethasone 17, 21-diproprionate". There is no example at all in the disclosure which can support the claimed invention.

In [0022] applicant describe about two separate dosage however, there is no example or guidance how this really works.

The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to one skilled in the art that the inventor had the possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claimed language. See *In re Kaslow*, 707 F 2d 1366, 1375 (Fed. Cir. 1983).

The written description requirement prevents applications from using the amendment process to update the disclosure in their disclosures (claims or specification) during the pendency before the patent office. Otherwise applicants could add new matter to their disclosures and date them back to their original filing date, thus defeating an accurate accounting of the priority of the invention. See 35 USC 132. The function of description requirement is to ensure that the inventor had possession, as of filing date of the application relied on, the specific subject matter claimed by him.

See *Genetech,* 108 F 3d 1361, 1365 (Fed. Cir. at 1366, 78, 1999).

Claim 1 of the present application

A method of treating a human patient with a form of cancer selected from the group consisting of leukemia, lymphoma and myeloma who has received an allogeneic hematopoietic cell transplant, comprising administering to said patient at least two oral dosage forms an amount of beclomethasone 17, 21-diproprionate, the dosage amount being capable of maintaining a graft-

versus-leukemia reaction and eliminating or reducing the number of cancer cells in the blood of said patient.

Applicant is kindly requested to explain the issue.

See MPEP 2163.06

Double Patenting Rejection

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1 and 4-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,096,731. Although the conflicting claims are not identical, they are not patentably distinct from each other because in instant application applicants are claiming a method of treating a patient with cancer to reduce symptoms of GVHD by using beclomethasone-17, 21-dipropionate as in claim 1.

Claimed invention in US '731 is drawn to a method for preventing tissue damage associated with GVHD by corticosteroid for a period of time following transplantation and prior to symptoms associated with graft-versus-host diseases (GVHD). Specific use of corticosteroid beclomethasone is claimed in claims 13-27, 39 and 40. The method is useful for preventing tissue damage (especially inflammation of the intestinal mucosa or small bile ducts or destruction of the intestinal mucosa) associated with (GVHD) following hematopoietic cell transplantation (especially of HLA-mismatched hematopoietic cells, unrelated donor hematopoietic stem cells, umbilical vein hematopoietic stem cells or peripheral blood stem cells) (all claimed). The method is also useful following intestinal or liver transplantation. The reference teaches that a patient with an underlying disease is treated for that disease with a form of therapy that includes the intravenous infusion of hematopoietic cells from an allogeneic donor. Within two days after the donor hematopoietic cells have been infused, the patient takes by mouth medication in the form of eight capsules of BDP per day, 1 mg per capsule, half of which are plain gelatin capsules that dissolve in acidic stomach fluid, the other half being gelatin capsules coated with a material that dissolves in the alkaline fluid of the small intestine and/or colon. **The BDP capsules are taken on a daily basis (eight per day) for 80 days** following the

infusion of the hematopoietic cells. After the 80 day period is over, the daily dose of BDP capsules is decreased by 50% for the ensuing 7 days (i.e., four capsules per day), then by an additional 50% for the next 7 days (i.e., two capsules per day), and then discontinued. Claimed invention is obvious over the claims of the issued patent. Specification of "731 teaches presently claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonald et al., AN 1998323484 MEDLINE; DN PubMed ID: 9649455; Gastroenterology, 1998 July; 115 (1), 28-35. The reference teaches an effective treatment of for intestinal graft-versus-host disease (GVHD) by beclomethasone dipropionate (BDP). Beclomethasone dipropionate a topically active steroid, is the effective treatment for intestinal graft-versus-host disease (GVHD) in a phase I study. The aim of this study was to compare the effectiveness of oral EDP to that of placebo capsules in treatment of intestinal GVHD. The reference further teaches that sixty patients with anorexia and poor oral intake because of intestinal GVHD were randomized to receive prednisone (1 mg.kg-l.day-1) plus either oral BDP (8 mg/day) or placebo capsules. Initial responders who were eating at least 70% of caloric needs at **evaluation on day 10 continued to take study capsules for an additional 20 days** while the prednisone dose was rapidly tapered.

The primary end point was the frequency of a durable treatment response at day 30 of treatment. The initial treatment response at **day 10** was 22 of 31 (71%) in the BDP/prednisone group vs. 16 of 29 (55%) for the placebo/prednisone group. The durable treatment response at **day 30** was 22 of 31 (71%) vs. 12 of 29 (41%), respectively (P = 0.02). CONCLUSIONS: The combination of oral BDP capsules and prednisone was more effective than prednisone alone in treating intestinal GVHD. Oral BDP allowed prednisone doses to be rapidly tapered without recurrent intestinal symptoms.

Furthermore, the reference teaches that oral BDP allowed **more doses** to be rapidly tapered without recurrent intestinal symptoms. See the abstract.

Instant claims differ from the reference in claiming to reduce or eliminate the symptoms while maintaining GVL reaction. The reference does not disclose about maintaining GVL reaction effective to eliminate or reduce the number of cancer cells in the blood of the said animal. It is assumed and inherent that when the symptoms are reduced GVL would be maintained.

It would have been obvious to one skilled in the art at the time of invention to treat the patients having GVHD by beclomethasone 17, 21-dipropionate one or more doses because prior art teaches the same method. Since the treatment is being done to the same population by the same compound it would maintain the GVL reaction as claimed. The results presented would have been expected in view of the teachings of the prior art of record.

Normally, change in temperature, concentration, or both, is not a patentable modification; however, such changes may impart patentability to a process if the ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from results of prior

art; such ranges are termed "critical" ranges, and applicant has burden of proving such criticality; even though applicant's modification results in great improvement and utility over prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art; more particularly, where the general conditions of the claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation. In re Aller et al. 105 USPQ 233.

It is well established that merely selecting proportions and ranges is not patentable absent a showing of criticality. In re Becket, 33 U.S.P.Q. 33 (C.C.P.A. 1937). In re Russell, 439 F.2d 1228, 169 U.S.P.Q. 426 (C.C.P.A. 1971).

In absence of any criticality and/or unexpected results instant invention is considered obvious over the prior art. See MPEP § 716.02 -§ 716.02(g) for a discussion of criticality and unexpected results.

See KSR Supreme Court of United States Decision (Decided April 30, 2007, KSR INTERNATIONAL CO. v. TELEFLEX INC. et al. No. 04-1350) where it states that (1) "However, the issue is not whether a person skilled in the art had the motivation to combine the electronic control with an adjustable pedal assembly, but whether a person skilled in the art had the motivation to attach the electronic control to the support bracket of pedal assembly". (2) "the results of ordinary innovation are not the subject of exclusive rights under the patent laws". In the present case the method as claimed would have been obvious to one skilled in the art at the time the invention was made.

The specification does not contain any example containing claimed two oral dosage forms for the said method of treatment.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Response to Remarks

Arguments were fully considered but are not found persuasive. STORB et al was withdrawn because Applicant argued that it does not specifically teach the selective cancer as presently claimed. However, McDonald reference inherently teaches that when the symptoms are reduced GVL would be maintained. The reference further teaches that sixty patients with anorexia and poor oral intake because of intestinal GVHD were randomized to receive prednisone (1 mg.kg-l.day-1) plus either oral BDP (8 mg/day) or placebo capsules. Initial responders who were eating at least 70% of caloric needs at **evaluation on day 10 continued to take study capsules for an additional 20 days** while the prednisone dose was rapidly tapered. The primary end point was the frequency of a durable treatment response at day 30 of treatment. Therefore, the present invention is considered obvious for the reasons cited above.

All the rejections are maintained.

No dosage has been used by Applicants to determine the amount of BDP taken per day.

Declaration

- The declaration filed by Applicants was not found persuasive because no criticality of invention was seen. All the data would have been expected in view of the teachings of the

prior art at the time the invention was filed. The claimed invention is considered a routine experimentation of the teaching of the prior art. Since the same compound, which is used for GVHD for the same population, maintains GVL no criticality of the invention was noted. The results shown about the doses, control of GVHD and better survival as summarized especially in sections 19-22 of the declaration are convincing however, it is unclear what is new in the instant claims, which was not previous claimed and/or taught by the prior art cited by the Examiner. Prior does teach "more doses" meaning that more than one.

- The disclosure does not contain any example or teaching for the claimed subject matter.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SABIHA QAZI, PH.D
PRIMARY EXAMINER